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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,009	05/30/2001	Hisashi Kashima	JP920000069US1	8419

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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
09/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/870,009	KASHIMA ET AL.	
	Examiner	Art Unit	
	Michael Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/31/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5, 8-12, 15, 17-27, and 30-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5, 8-12, 15, 17-27 and 30-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/22/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 12/31/2007 has been entered.

Claim Objections

Claims 5, 8 and 15 are objected to because of the following informalities: the claims are sentences and thus should begin with an article, such as "A", "An", "The", etc. Appropriate correction is required.

Claim 23 is objected to because of the following informalities: "and is" in the second line should be "is.". Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 8-12, 15, 17-27 and 30-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Mendez et al (Nat. Genet., 1997) as evidenced by Albertson et al (1990) and the pYAC4 GenBank entry (1995).

The claims specify a "value-added gene" and a "watermark", two terms not typically used in the relevant art and which are not defined in a limiting manner by the instant disclosure. The specification indicates that a "value-added gene" is a gene that adds value to an organism or cell, see page 1 of the specification. This is a broad term, and can literally be applied to any DNA sequence added to a cell or organism because the relative value of a cell or organism is determined by the wants and needs of the skilled artisan, and will be specific for the particular problem at hand. A simple example is adding a transgene of choice, human erythropoietin, for example, to a cell line; the cell line is then more valuable to the skilled artisan for the production and expression of the therapeutic protein erythropoietin. Regarding "watermark", the specification indicates this is a DNA sequence carrying predetermined information (page 11, first ¶), such that the DNA is distinguishable. Thus, this limitation can also be literally any DNA sequence that is known to the skilled artisan and is present in the DNA molecule.

Mendez et al teach yeast artificial chromosomes (YACs) comprising certain human immunoglobulin loci, which loci each comprise several genes that encode the heavy or light chains of human antibodies. See the abstract, Fig. 1 and the corresponding figure legend. The YACs also comprise centromeric and telomeric sequences (circles and arrows, respectively, in Fig. 1). These YACs were inserted into the genome of mouse embryonic cells which were used to create transgenic mice bearing one of the YACs in the germline, then bred to generate mice comprising both YACs, such mice being able to express fully human antibodies in response to a

given antigen (page 148, second column, first full ¶ to page 151). Thus, the YACs and mice comprised "value-added genes", (any one of the heavy or light chain genes found within the YACs) according to the specification, as the mice could be used to generate fully human antibodies - an important milestone towards antibody therapy of disease (page 146, first column, second ¶). Furthermore, the YACs comprised watermark sequences according to the specification, that is, predetermined sequences not found in the mouse chromosome such as the YAC centromeric and telomeric sequences, which were inherently known to the skilled artisan for at least one of the YACs (based upon the pYAC4 vector, the sequence of which was known by the latest in 1995, see the GenBank entry for pYAC4 (provided); page 154, second column, fourth full ¶ of Mendez et al referencing Alberston et al, 1990, also provided). These are yeast DNA sequences, such as the ARS1, CEN4, and Tetrahymena telomeric elements not naturally found in human or murine DNA (pages 3-4 of the pYAC4 entry). Sequences within the YACs were used in Southern blotting experiments to determine the integration of the YACs into ES genomes (Figs. 2 and 3), but not in WT mouse genomes. Thus, any of the centromeric or telomeric sequences (or selection markers such as *neo, LYS2, or HPRT*, see Fig. 1), or any of the heavy or light chain genes other than the one considered to be the "value-added gene" could be considered a watermark according to claims 5, 8, 11, 12, and 15. The plurality of sequences recited in claims 9, 10 and 18-20 is considered to be the telomeric and centromeric sequences (of which there are three in both YACs), each of which has within different "patterns", or DNA sequences. For example, the ARS1 sequence in pYAC4 is considered to be from nucleotides 9629-10467 and the CEN4 sequence from 10802-10908 (see page 4 of the pYAC4 GenBank entry). Each of these is an example of a "watermark" according to the claims, or, sequences

found within these DNA elements could be considered "watermarks"; e.g. the ARS1 element is 838 bp long and thus comprises at least eight 100 bp DNA subsequences that can serve as "watermarks" according to the instant specification, which estimates that sequences of only 30 bp are sufficient to act as watermarks (page 22).

Regarding claim 17, the YACs are considered a single molecule.

Regarding claim 21, because the YAC sequences were passed through the mouse germline, they are considered copy tolerant.

Regarding claims 22, 26 and 33 these are product by process claim (as are all the claims, e.g. they recite the introduction of a gene by "one of selective breeding, cultivation, and gene manipulation") and thus are not limited by the recited method steps, only the structure implied by the steps. See MPEP 2113. The DNA structure, i.e. the DNA sequence, of the watermark sequences set forth above does not change whether they are inserted "randomly" or non-randomly (i.e. claim 27), or by one of the sources listed in claim 5.

Regarding claim 23, none of the sequences set forth above that are considered to be watermarks was generated through mutation.

Regarding claim 24, if the *HPRT* gene is considered to be the watermark, then it was inherently associated with a promoter because this selection marker was expressed (Fig. 1, page 148, second column, first full ¶, page 155, first column, second full ¶).

Regarding claim 25, any of the above watermarks could be detected with the appropriate complementary DNA, as short as 20-25 bp, i.e. a PCR primer, or longer sequences used in Southern blotting.

Regard claims 27 and 30, the centromeric and telomeric sequences (and literally any other sequence set forth above as a watermark) of the YACs are correlated to the YACs because they are found within the YACs and not within the human and/or murine genome. The skilled artisan could identify them upon examining the DNA, given the known information about the YACs set forth in Mendez et al and the pYAC4 GenBank entry.

Regarding claim 31 and 34, Mendez et al teach that functional human antibodies were expressed from the transgenic mice (see above), thus, these value-added genes comprised transcription control sequences and protein coding sequences.

Regarding claims 32 and 34, the centromeric and telomeric sequences set forth above do not encode protein or control transcription (simply put, they are origins of DNA replication).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5, 8-12, 15, 17-27 and 30-34 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. **This rejection is maintained for reasons set forth in the Examiners Answer dated 9/8/2006 and the BPAI Decision dated 10/29/2007 (Appeal 2007-1627).**

To reiterate, the claims encompass viral genomes comprising HIV LTRs (long terminal repeats) or the genomes of cells infected with HIV. In addition, any animal or person infected with such a virus inherently encompasses the LTRs, thus the cells recited in the instant claims encompass humans and animals. As the DNA and cells recited in the instant claims are not

limited to be different from those existing in nature; i.e. they are not limited to be "purified" or "isolated," claims 5, 8-12, 15, 17-27, and 30-34 encompass naturally existing organisms and humans, and are thus directed to nonstatutory subject matter.

Regarding the claim amendments, as set forth above a "value-added gene" is determined by the purpose of the skilled artisan, and can be literally any given gene desired to be studied or used for experimental procedures. Thus, HIV-infected cells have "value-added genes" because they are valuable to the HIV researcher or clinician as valuable reagents used as positive controls, as a source of the virus, or of viral proteins. Regarding the "watermark" limitation, the HIV LTR is considered a watermark according to the instant specification, for reasons set forth in the BPAI decision (pages 5-8 of Appeal 2007-1627), and for reasons set forth above. Regarding the limitation that the gene is added by one of several sources (e.g. breeding), these are product by process limitations and are treated as above. thus are not limited by the recited method steps, only the structure implied by the steps. See MPEP 2113. The DNA structure, i.e. the DNA sequence, of the genes does not change depending upon the nature of how they are added or provided.

Response to Arguments

Applicants present no new arguments regarding this rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1633

/Michael Burkhart/
Primary Examiner, Art Unit 1633